(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property **Organization** International Bureau





(43) International Publication Date 15 July 2004 (15.07.2004)

PCT

(10) International Publication Number WO 2004/058722 A1

(51) International Patent Classification7: C07D 231/12, A61K 31/415, A61P 7/02, C07D 405/12, 413/12, 401/12,

403/12, 417/12

(21) International Application Number:

PCT/US2003/040844

(22) International Filing Date:

22 December 2003 (22.12.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 60/436,326 24 December 2002 (24.12.2002) US 60/464,992 23 April 2003 (23.04.2003)

(71) Applicant (for all designated States except US): ARENA PHARMACEUTICALS, INC. [US/US]; 6166 Nancy Ridge Drive, San Diego, CA 92121-3223 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): TEEGARDEN, Bradley [US/US]; 11933 Windom Peak Way, San Diego, CA 92131 (US). JAYAKUMAR, Honnappa [US/US]; 13323 Caminito Ciera, #107, San Diego, CA 92129 (US).

STRAH-PLEYNET, Sonja [SI/US]; 12542 Darkwood Road, San Diego, CA 92129 (US).

(74) Agents: SPRUCE, Lyle et al.; Arena Pharmaceuticals, Inc., 6166 Nancy Ridge Drive, San Diego, CA 92121-3223 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DIARYLAMINE AND ARYLHETEROARYLAMINE PYRAZOLE DERIVATIVES AS MODULATORS OF 5HT2A

$$\begin{array}{c|c}
R_4 & R_5 \\
R_1 & N \\
R_5 & N \\
R_3 & R_{3a}
\end{array}$$
(A)

(57) Abstract: One aspect of the present invention relates to certain diarylamine and arylheteroarylamine pyrazole derivatives of Formula (A) and pharmaceutical compositions that modulate the activity of the human 5HT2A serotonin receptor. Compounds and pharmaceutical compositions are directed to methods useful in the prophylaxis or treatment of reducing platelet aggreagation, sleep disorders, coronary artery disease, myocardial

infarction, transient ischemic attack, angina, stroke, atrial fibrillation, reducing the risk of blood clot formation, asthma or symptoms thereof, agitation or a symptom, behavioral disorders, drug induced psychosis, excitative psychosis, Gilles de la Tourette's syndrome, manic disorder, organic or NOS psychosis, psychotic disorder, psychosis, acute schizophrenia, chronic schizophrenia and NOS schizophrenia and related disorders. Another aspect of the present invention is directed to the method of prophylaxis or treatment of 5HT2A serotonin receptor mediated disorders in combination with a dopamine D2 receptor antagonist such as haloperidol, administered separately or together.